WaveLight
Laser Technologie AG

ALLEGRETTO WAVE™

Scanning Spot LASIK Laser System

Procedure Manual

Information for professional use

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Using The ALLEGRETTO WAVE™ Procedure Manual

This manual provides information for the intended clinical use of the ALLEGRETTO WAVE Laser System.
Refer to the Operator Manual for the Laser Console and to the User's Manuals of the approved accessories for information regarding these components.

Carefully read and understand this manual and all related documents and instructions before using the ALLEGRETTO WAVE Laser System.

Observe all warnings, precautions and contra-indications as described in these documents.

Do not perform adjustments and procedures other than those described herein. Failure to do so may result in harm to patient and / or user.

Consult the Table of Contents, Appendices or Indices for specific information.
If you have questions that are not addressed in this manual, contact:

Lumenis Customer Hotline
(Business Card / Sticker)

TYPOGRAPHICAL CONVENTIONS

The following conventions are used in this manual for Warnings, Precautions and Notes:

WARNING

A Warning alerts the user to potential serious outcomes to the patient or the user.

CAUTION

Precautions alert the user to exercise special care necessary for the safe and effective use of the device.

NOTE

Notes provide user with helpful or supplementary information.

NOTICE TO USERS

RESTRICTIONS BY US FEDERAL LAW

CAUTION: US Federal law restricts this device to sale by or on the order by a physician or licensed eye care practitioner.

CAUTION: US Federal law restricts the use of this device to practitioners who have been trained in its operation, test and calibration and who have experience in the surgical management and treatment of refractive errors of the human eye.

RESTRICTIONS BY MANUFACTURER

There are no rightful claims to system upgrades in the event of the introduction of product improvements based on new technological developments.

CAUTION

Read and understand this Procedure Manual, the Operators Manual and all related manuals of the Laser System and its approved accessories before starting to use the ALLEGRETTO WAVE Laser System!

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2 SAFETY

2.1 General Warnings and Precautions

The ALLEGRETTO WAVE Laser System is a medical device currently designed for use in ophthalmology for the photorefractive treatments with the Laser In-Situ Keratomileusis ("LASIK") procedure. It is intended for use solely by the physicians trained in the use of this Laser System.

WaveLight medical lasers and accessories are intended solely for use by the physicians trained in the use of these instruments.

The system user alone is responsible for having sufficient medical knowledge for carrying out all surgical procedures. The user must be well versed in the therapeutic effects and possible dangers of the device and must possess the necessary skills to use it in conformity with the operating instructions contained in this manual.

Ensure that you have complied with all local, regional and governmental regulations pertaining to the use of Class IV lasers prior to using this device.

Only ALLEGRETTO WAVE Service Representatives or Service Representatives who have been specifically authorized by WaveLight Laser Technologie AG may service the Laser System.
Servicing or any form of manipulation of the system by non-authorized personnel will result in a termination of the warranty and nullification of any liability on the part of WaveLight Laser Technologie AG.

The ALLEGRETTO WAVE Laser System may only be operated with accessories or components that are approved, delivered or provided by WaveLight Laser Technologie AG specifically for the use with the ALLEGRETTO WAVE Laser System.

Do not operate the Laser System if any of the screens are dark or the display is distorted.

The ALLEGRETTO WAVE Laser System is a stationary device that must not be moved by the user.

After turning on the Laser System carefully go through the calibration tests and record the results in the laser logbook. The system has to be tested successfully before use. Failure to do so may result in harm to the patient (under - or over correction or de-centered ablation).

Call the ALLEGRETTO WAVE Service Representative to check the Laser System after exposure to any kind of shock that could have caused a misalignment of the optical elements. Misalignment after a shock exposure could result in non-satisfactory treatments.

Precautionary measures are to be employed in the handling and use of all accessories, disposable articles and agents that come into contact with patients to avoid exposure to pathogens.

Do not operate the laser system outside the environmental specifications provided in the Operators Manual.

Do not eat drink or smoke in the laser room.

During surgery, carefully monitor the laser ablation through the microscope. Stop depressing the Laser Foot Pedal immediately if the laser spots seem to fall only in one location or debris or liquid is visible on the ablated surface.

2.2 Patient Safety

All patients must be given the opportunity to read and understand the Patient Booklet and all of their questions must have been answered to the patients' satisfaction before giving the consent for Laser In-Situ Keratomileusis surgery (LASIK).

2.3 Laser Radiation Hazards

Eye and Skin Exposure

The ALLEGRETTO WAVE Laser System contains a Class IV laser. The integrated Excimer laser creates invisible UV laser radiation with 193 nm wavelength. The emission is pulsed with a repetition rate of 200 Hz. Each pulse has a pulse length of 10-20 ns. The average power is < 0.8 W.

This radiation is potentially hazardous to skin and to surface layers of the cornea. This radiation will not enter the eye and is not hazardous to posterior segment of the eye or to the crystalline lens.

Hazardous laser radiation will occur during the test procedures, treatment and service procedures. During user test procedures and treatments, the radiation leaves the Laser Aperture under the Microscope arm towards the headrest or the floor. The area of potential hazard is called the Nominal Hazard Zone (NHZ). As reflections may occur from instruments or devices brought into the laser beam, the entire laser room is considered to be the NHZ. The floor, ceiling, walls, closed doors and closed windows bound the hazard zone.

All personnel in the laser room should avoid direct laser radiation exposure to skin or eyes.

Laser Safety Eyewear

All personnel who are within the NHZ shall wear eye protection with a minimum optical density (OD) of 8.23 at 193 nm wavelength.

Additional Ocular Protection

Never substitute prescription eyewear for the appropriate laser safety eyewear, as severe eye damage could occur. Prescription eyewear can concentrate the laser light onto the eye and/or can be shattered by a high power density beam, possibly causing severe eye damage. Laser safety eyewear must be worn in addition to prescription eyewear.

Never look directly into laser aperture while the laser is powered. Severe eye damage could occur. Turn off the laser before inspecting any delivery system or laser components.

Laser Area

In addition to providing the required laser safety eyewear, take the following steps to secure the treatment room, or the controlled area:

To alert personnel before they enter the controlled area, place a warning sign on the outside of all treatment room doors when the laser is in use.

Close the treatment room doors during operation of the laser.

External door interlocks that automatically disable the laser when the treatment room door is opened may be installed.

Additional Safety Considerations

Laser light can be reflected off smooth metallic surfaces, even though they may be blackened.

CAUTION

Plastic instrumentation such as speculums or eye shields may melt when exposed to the laser beam, possibly resulting in chemical burns or noxious gases. Therefore, only surgical instruments approved for the use with lasers should be used.

Use of controls or adjustments or performance of procedures other than those specified herein may result in hazardous laser radiation exposure.

For further information regarding Laser Safety refer to the Operators Manual.

2.4 Airborne Contaminants

Laser Plume

Laser plume may contain viable tissue particulates.
The Laser Plume may be noxious to those who come into contact with it. The plume presents a possible biologic and pollution hazard and should be evacuated. Plume Evacuation has to be applied during every treatment.

Fluorine

The ALLEGRETTO WAVE Laser System is equipped with pressurized cylinder of ArF-Premix-Gas. Fluorine is one of the ingredients of the ArF-Premix-Gas mixture necessary for operating the excimer laser. The ALLEGRETTO WAVE ArF-Premix-Gas includes < 0.2 Vol. % Fluorine gas.
Fluorine gas is hazardous. Inhalation as well as eye and skin contact with fluorine should be avoided.

Keep the ArF Premix Gas Cylinder closed when the system prompts you to do so or when powering down the Laser Console. Fluorine can be detected by its pungent odor.

For further information regarding gas safety refer to the Operators Manual.

Ozone

A further potential danger consists due to the formation of ozone, which arises from the interaction of oxygen and either ultraviolet radiation or high voltage. Ozone can also be detected by its pungent odor. Purging the beam path with nitrogen reduces the formation of ozone in the laser system.

Further Information

For further information regarding safety against airborne contaminants, refer to the Operators Manual.

2.5 Protecting Non-target Tissues

Except during actual treatment and test procedures, the Laser Console must always be in Standby Mode. Maintaining the Laser Console in Standby Mode prevents accidental laser exposure if the Laser Foot Pedal is inadvertently depressed.

Only the person performing the surgery should have access to the Laser Foot Pedal. Use caution depressing the Laser Foot Pedal when it is in proximity to footswitches for other equipment. To avoid accidental laser exposure make sure the footswitch about to be depressed is the correct one.

2.6 Electrical Hazard

Never open the protective covers of Laser Console and accessories. Opening the covers can expose the user to high voltage components, the laser resonator and possible laser radiation. Only WaveLight-certified ALLEGRETTO WAVE Service Representatives shall work inside the Laser Console and inside the accessories.

The area around the Laser Console, Foot Pedal Unit and any of the accessories should be kept dry. Do not operate the laser if any of the cords are faulty or burned. The laser should undergo routine inspection and maintenance per WaveLight manufacturer's recommendations and institutional standards.

2.7 Fire Hazards

Do not use this device in the presence of flammables or explosives, such as, but not limited to, volatile anesthetics and alcohol. An explosion and/or fire could occur.

2.8 Electro-Magnetic Radiation Hazards

The device has been successfully tested for electromagnetic conformity according to IEC 601 standard (International standard for medical laser systems).

Despite adherence to all applicable EMC requirements, collateral influence of laser system and other electronic devices cannot be ruled out entirely. The use of any kind of cellular device in the laser room and in the vicinity of the laser during test and treatments is not allowed.

Although it is not contraindicated to treat patients with implantable medical devices, the effects are unknown.

On account of possible risk of interference while the laser is in operation, persons with implanted devices such as, but not limited to pacemakers or defibrillators may not be present in the laser room during operation.

Effects on embryos are unknown. Pregnant women may not be present in the laser room while the laser is in operation.

3 DEVICE DESCRIPTION

The ALLEGRETTO WAVE is a scanning spot Excimer Laser System used in refractive surgery for photorefractive treatments with the Laser In-Situ Keratomileusis (LASIK) technique.

The excimer laser creates a radiation of 193 nm wavelength. This radiation is able to ablate corneal tissue in very thin layers without damage or thermal alteration of collateral tissue. The ablation effect is threshold dependent - the energy per irradiated area, known as Fluence, has to be above a certain threshold to ablate corneal tissue. Below the threshold the radiation will cause heating instead of ablation.

The laser radiation is used to change the front shape of the corneal lens by ablating tissue. This sculpting has to be done with very high precision in order to achieve a new corneal lens shape with the desired smoothness of surface and precision of optical power. Every single laser pulse (spot) has to meet very high requirements regarding precision of ablated depth, volume and spot position.

The ALLEGRETTO WAVE Laser System consists of a combination of features including several internal energy control mechanisms and external test procedures to provide the right energy and fluence per laser pulse. The fast Eyetracker for determining eye position and a precise scanner motor for positioning the laser spot enable precise placement of every laser spot even when the eye is moving or having saccades. In addition, the Eyetracker offers an automatic centration of the ablation to avoid unintended decentration of the correction zone.

The Gaussian shaped energy distribution within the laser beam and a small ablation spot of approximately 1 mm assure the desired contour precision and high surface smoothness of the newly shaped corneal curvature. The ablation profiles that are used in the ALLEGRETTO WAVE are "WaveFront Optimized" meaning that the initial profiles, which can be calculated mathematically, were refined by empirical research with a wavefront aberrometer. Refer to section 10.3 for detailed information about ablation profiles.

Due to the small spot diameter used in the ALLEGRETTO WAVE, the excimer laser beam source is compact with low laser gas volume and minimal laser gas consumption.

During the treatment thousands of laser pulses have to be delivered to the cornea in a complex pattern. As the excimer laser is operated with a high repetition rate of 200 pulses per second, treatment times are short.

For treatments at least the following components of the system have to be operated:

Laser Console	- containing operating elements, laser head, optical transmission system, energy and system controls, eyetracker, scanner motors, gas supply, focusing and fixation lights, system software and ablation profiles with scanning spot patterns, operating microscope with illumination and test systems.
Patient Bed	- with moving motors and bed control
Eyetracker Monitor	- showing the tracked pupil / eye
Notebook Computer	- containing software for programming treatment parameters
Plume Evacuator	- to remove ablation plume during treatment

Optional accessories, such as slit lamp, may be applied for higher comfort.

A microkeratome of the physician's choice is utilized to create the flap before the laser portion of the treatment can be conducted.

4 INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS AND ADVERSE EVENTS

4.1 Indications for Use

The ALLEGRETTO WAVE Laser System is indicated for use in Laser In-Situ Keratomileusis (LASIK) treatments for:

- the reduction or elimination of myopia of up to –12.0 diopters (D) of sphere and up to - 6.0 D of astigmatism at the spectacle plane;
- the reduction or elimination of hyperopic refractive errors up to +6.0 D of sphere with and without astigmatic refractive errors up to 5.0 D at the spectacle plane, with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D;
- patients who are 18 years of age or older; and
- patients with documentation of a stable manifest refraction defined as ≤ 0.5 D preoperative spherical equivalent shift over one year prior to surgery, exclusive of changes due to unmasking latent hyperopia.

4.2 Contraindications

LASIK treatments are contraindicated in:

- pregnant or nursing women;
- patients with a diagnosed collagen vascular, autoimmune or immunodeficiency disease;
- patients with diagnosed keratoconus or any clinical pictures suggestive to keratoconus; and
- patients who are taking one or both of the following medications: isotretinoin (Accutane®[1]); amiodarone hydrochlorid (Cordarone®[2]).

[1] Accutane® is a registered trademark of Hoffmann-La Roche Inc.
[2] Cordarone® is a registered trademark of Sanofi-Synthelabo Inc.

4.3 Warnings

LASIK treatment is not recommended in patients who have:

- systemic diseases likely to affect wound healing, such as connective tissue disease, insulin dependent diabetes, severe atopic disease or an immunocompromised status;
- a history of Herpes simplex or Herpes zoster keratitis;
- significant dry eye that is unresponsive to treatment; and
- severe allergies.

4.4 Precautions

General

Safety and effectiveness of the ALLEGRETTO WAVE Laser System has not been established for patients:

- with progressive myopia, hyperopia and/or astigmatism, ocular disease, previous corneal or intraocular surgery, or trauma in the ablation zone;
- with corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage;
- with residual corneal thickness after ablation of less than 250 microns due to an increased risk for corneal ectasia;
- with history of glaucoma or ocular hypertension of > 23 mmHg;
- taking the medication sumatriptan succinate (Imitrex®[3]);
- under 18 years of age;
- over the long term (more than 12 months after surgery);
- with media problems, corneal, lens and/or vitreous opacities including, but not limited to, cataract;

[3] Imitrex® is a registered trademark GlaxoSmithKline Inc.

- with iris problems including , but not limited to, coloboma and previous iris surgery compromising proper eyetracking;
- taking medications likely to affect wound healing including, but not limited to, antimetabolites;
- for treatments with an optical zone below 6.0 millimeters and above 6.5 millimeters in diameter. While the ALLEGRETTO WAVE has the potential for additional ranges of optical and ablation zones, no information is available regarding their level of safety and/or effectiveness;
- with myopia greater than -12 **Diopters** or **astigmatism** greater than 6 **Diopters**; and
- with hyperopia greater than +6.0 **Diopters** or **astigmatism** greater than 5 **Diopters**.

Pupil sizes should be evaluated under mesopic illumination conditions. Effects of treatment on vision under poor illumination cannot be predicted prior to surgery. Some patients may find it more difficult to see such in conditions as very dim light, rain, fog, snow and glare from bright lights. This has been shown to occur more frequently in the presence of residual refractive error and perhaps in patients with pupil sizes larger than the optical zone size.

The refraction is determined in the spectacle plane, but treated in the corneal plane. In order to determine the right treatment program to achieve the right correction, assessment of the vertex distance during refraction test is recommended.

Preoperative evaluation for dry eyes should be performed. Patients should be advised of the potential for dry eyes post LASIK surgery.

Patient Selection

In addition to contraindications, warnings and general precautions the following should be considered in order to find good candidates for LASIK and to get sufficient information for the treatment plan:

- A complete baseline exam including, but not limited to, cycloplegic refraction within 60 days prior to surgery is necessary. A slit lamp exam has to be performed. The status of the lens has to be evaluated to ensure that neither nuclear sclerosis nor other lens opacities are present. These opacities may adversely affect final visual result. Dilated fundus exam by indirect ophthalmoscopy has to be performed, as retinal pathology is more likely in patients with myopia.

- Optical nerve and intraocular pressure have to be examined as glaucoma is more common in myopic than emmetropic subjects. If elevated pressure or signs of glaucomatous damage are found, topical steroids should be used only under careful medical supervision or the patient should not be treated.

- In order to exclude corneal abnormalities careful videokeratography (topography) is essential.

- Contact lens wearers must discontinue wearing hard or gas permeable lenses for at least 3 weeks and soft lenses for at least 3 days **prior to preoperative evaluation**.

- Contact lens wearers must also discontinue wearing hard or gas permeable lenses for at least 3 weeks and soft lenses for at least 3 days **prior to surgery**.

- The patient must be able to lie flat in a supine position

- Topical or local anesthesia must be tolerated.
- The patient must be able to fixate steadily.
- The patient must be able to understand and give the informed consent and sign the informed consent form.
- All alternatives to the LASIK procedure for correcting myopia, hyperopia and/or astigmatism by spectacles, contact lenses and other surgical procedures such as radial keratotomy, automated lamellar keratoplasty or clear lens exchange should be clearly communicated and understood by the patient.

Procedure

The determined patient and eye data have to match with the patient presenting and with the eye prepared for surgery. Make sure that treatment parameters are precisely transferred from the files to the laser system. A double check with the patient and assisting personnel is recommended. It is the sole responsibility of the operating surgeon to ensure that all data is accurate.

Carefully clean and prepare the microkeratome according to its manuals. Make sure that the blade is free of burrs and nicks. Check if the chosen plate thickness matches with the intended flap thickness.

Instruct patients not to wear makeup as this poses risk for contamination of the stromal interface. Patients must not use perfumes, After Shave, Eau de Cologne or other substances applied to the skin containing alcohol.

Aromatic substances and solvents including, but not limited to alcohol, fresh glue and paint should not be noticeable at the laser aperture, because these substances may absorb energy of the laser pulses and therefore may cause undercorrections.

Strong disturbances of the air between the laser aperture and the patient's head during laser ablation must be avoided. Switch off any ventilation device causing a noticeable airflow during ablation, with exception of the Plume Evacuator of the Laser System. Instruct personnel not to move around and keep doors and windows closed during ablation. Uncontrolled airflow may have an effect on the quality of the ablation.

Potentially noisy devices such as telephones that may cause a sudden sound during the procedure should be switched off. Sudden noise may distract surgeon and / or patient.

Medications likely to dilate or constrict the pupil should not be given during the last 6 hours prior to surgery as the Eyetracker will not be able to track pupils of less than 1.5 mm and more than 8.0 mm diameter.

Check that the patient is able to see the green blinking fixation light and to discern it from other light sources around the laser aperture (See Section 10.4 for images of patient view).

Perform an External Energy Check according to the Operators Manual prior to treating a new patient. Repeat the test if more than 30 minutes have elapsed before the treatment is begun.

Head alignment in order to apply cylinder treatment in the right axis is essential.

If laser ablation is interrupted, the parameters remain in the system and the system will proceed with the ablation pattern exactly at that point, at which the treatment was interrupted. The progress of the ablation procedure is indicated in the LCD Display of the Laser Console.

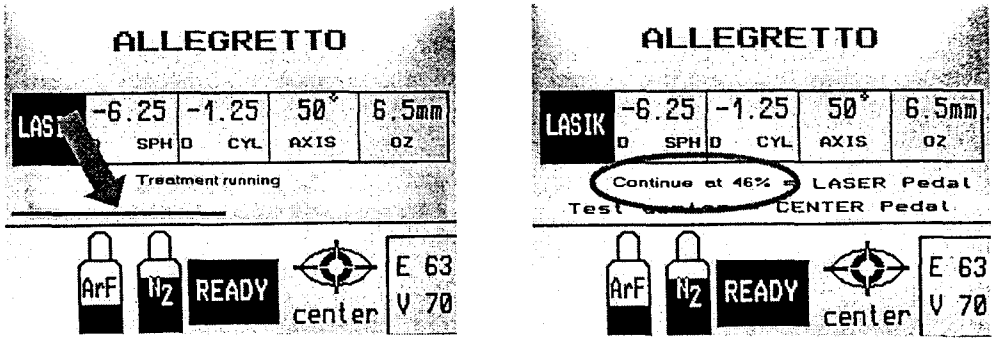


Figure 1: Progress Indicators

If for any reason a treatment has to be terminated before ablation was completed, the percentage of treatment accomplished has to be recorded and kept in the patient files.

CAUTION

Aborted treatment

If the treatment is aborted, treatment parameters and progress information are lost. Reasons may include power loss or manual abortion. The system offers no procedure to finish the treatment at a later time.

During ablation spherical and astigmatic error are treated separately. The spherical portion of the refractive treatment is applied first; the astigmatic portion follows immediately without interruption. In myopic treatments both ablation portions are enrolled by creating the full amount of intended correction during the first few seconds, but in a diameter smaller than the full Optical Zone. During the course of the ablation the zone already corrected is enlarged to the programmed Optical Zone diameter. The currently achieved diameter with full correction is not indicated.

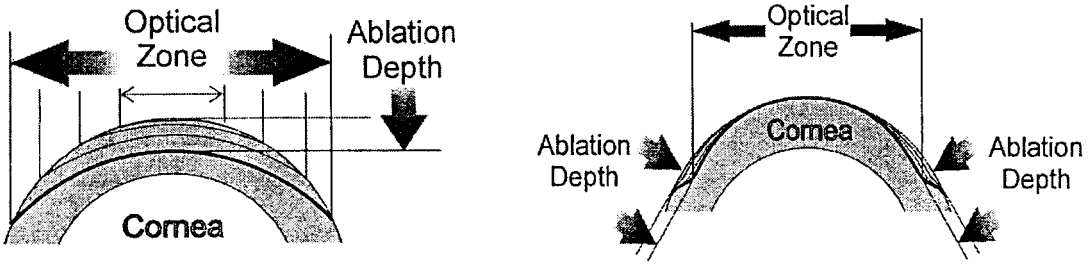
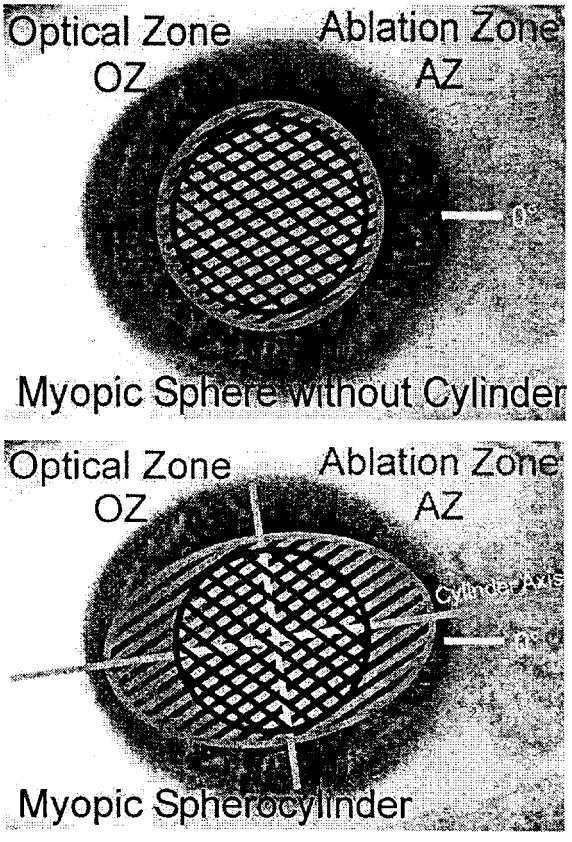


Figure 2: Evolution of Ablation Myopia treatment (left) and Hyperopia treatment (right)

In Hyperopic treatments, the profile is corrected over the full optical zone and only depth is increased. The currently achieved depth is not indicated.

Do not perform a laser ablative treatment on a stromal surface compromised due to cutting problems with the microkeratome, such as buttonhole, step profile or severe incomplete cut smaller than the intended Optical Zone.

Keep the stromal surface dry and clean during ablation. Prevent liquid or blood from running towards the Ablation Zone. Liquid and debris will shield the stromal surface against ablation. Irregular ablations will most likely result. If liquid or blood reaches the Optical Zone, irregular ablations may lead to deviation of the best possible clinical results.



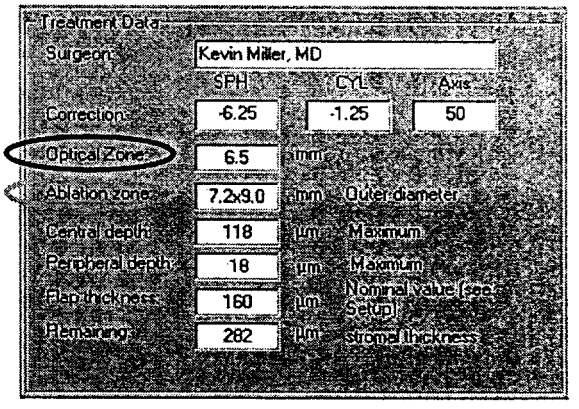


Figure 3: Optical and Ablation Zone Myopic Treatment

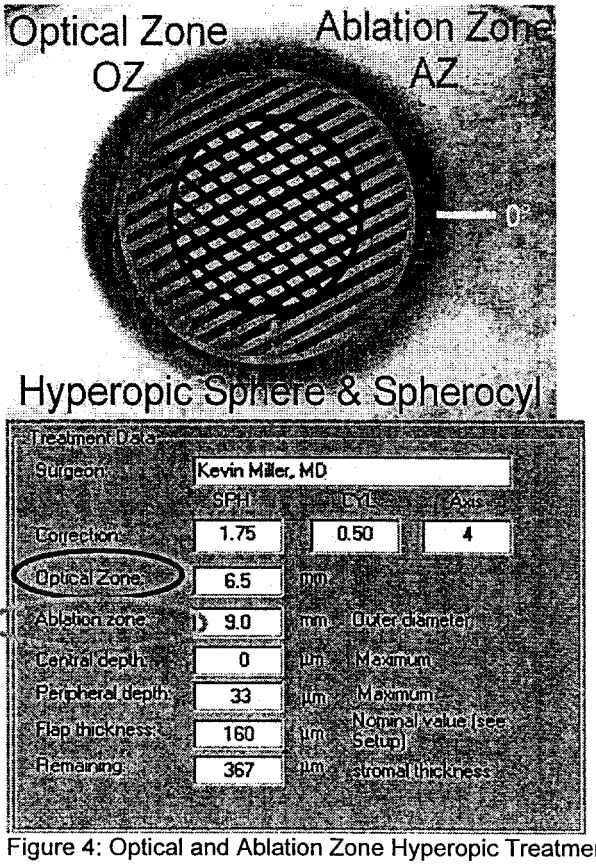


Figure 4: Optical and Ablation Zone Hyperopic Treatment

Do not move instruments across or in the area of the intended Optical Zone during laser ablation. The instrument may shield stroma partially against ablation. Resulting irregular ablations may lead to a deviation of the best possible clinical result. Optical and Ablation Zone diameters are indicated in the Notebook Computer screen. The LCD display of the Laser Console shows the Optical Zone diameter only.

5.2 Hyperopia Study

The Sponsor performed a clinical study of the WaveLight ALLEGRETTO WAVE Excimer Laser System at ten U.S. clinical sites under the auspices of an Investigational Device Exemption (IDE) G990317. The data from this study served as the basis for the approval decision. Specifically, safety and effectiveness outcomes at 3 months postoperatively were assessed, as stability was reached at that time. Outcomes at 6 and 12 months postoperatively were also evaluated for confirmation of stability. The IDE study is described in detail as follows.

Study Objectives Hyperopia

The objectives of the study were to determine the safety and effectiveness of the WaveLight ALLEGRETTO WAVE Excimer Laser System for LASIK treatment of hyperopic refractive errors up to +6.0 D with and without astigmatic refractive errors up to 6.0 D, with a maximum manifest refraction spherical equivalent of +6.0 D.

Study Design Hyperopia

The study was a prospective, non-randomized, 10 center, 11 surgeon study where the primary control was the preoperative status of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

Inclusion and Exclusion Criteria Hyperopia

Subjects in the LASIK for hyperopia and hyperopic astigmatism study must have met all of the following inclusion criteria to qualify for enrollment:

- Subjects must be undergoing LASIK surgery for the correction of hyperopia.
- Intended treatment from 0 to +6.0 D of spherical equivalent hyperopia or hyperopia with astigmatism, with up to +6.0 D of spherical component and up to 6.0 D of astigmatic component. (All refractions measured at the spectacle plane).
- Subjects must have bilateral physiologic hyperopia.
- BSCVA of 20/40 or better in each eye.
- Subjects must have had a stable refraction (0.5 D or less change in MRSE) for the last 12 months, objectively documented (by previous clinical records, eyeglass prescriptions, etc.), exclusive of changes determined by the investigator to be due to unmasking of latent hyperopia.
- Subjects who are contact lens wearers must have hard or gas permeable lenses discontinued for 3 weeks and soft lenses discontinued for 3 preoperative evaluation.

- Subjects must be at least 18 years of age.

- Corneal topography must be normal, as judged by the operating investigator.
- Subjects must sign a written Informed Consent form acknowledging their awareness of their participation in this study, the alternative treatments available, the risks involved, and the investigative nature of LASIK, and other issues that conform to the standard of care for Informed Consent practices.

- Subjects must be able to return for scheduled follow-up examinations for 24 months after surgery.

Subjects with the following conditions were not eligible for enrollment in the LASIK for hyperopia and hyperopic astigmatism study:

- Subjects with anterior segment pathology

- Subjects with residual, recurrent or active ocular disease

- Subjects who have undergone previous intraocular or corneal surgery involving the stroma in the eye to be operated.

- Subjects who have a history of herpes keratitis

- Subjects with diagnosed autoimmune disease, systemic connective tissue diseases or atopic syndrome, diabetes mellitus, or taking systemic medications (i.e., corticosteroids or antimetabolites) likely to affect wound healing

- Subjects with unstable central keratometry/topography readings with irregular topography patterns or keratometry mires, including signs of keratoconus.

- Subjects with known sensitivity to study medications.

- Subjects with intraocular pressure of > 23 mm Hg by Goldmann applanation tonometry, a history of glaucoma, or glaucoma suspect.

- Women who are pregnant or nursing or who plan to become pregnant over the course of their participation in this investigation.

- Participation in other ophthalmic clinical trials during this clinical investigation

- Subjects with colobomas of the iris or other irregularities of the pupil margin.

- Gonioscopic angle measurement of Grade 2 or less, or occludable angle as judged by the investigator.

Study Plan, Patient Assessments, and Efficacy Criteria Hyperopia

Subjects were evaluated preoperatively and postoperatively at 1 day, 1 month, 3 months, 6 months, 9 months, 1 year, 18 months and 2 years. Preoperative objective measurements included: uncorrected distance and near visual acuity, manifest refraction, distance best spectacle corrected visual acuity, cycloplegic refraction, applanation tonometry, slit lamp examination, pupil size measurement in photopic and scotopic conditions, central keratometry, computerized corneal topography, pachymetry, dilated fundus examination, and patient questionnaire.

Postoperatively, objective measurements included: uncorrected distance and near visual acuity, manifest refraction, distance best spectacle corrected visual acuity, cycloplegic refraction, applanation tonometry, slit lamp examination, central keratometry, computerized corneal topography, dilated fundus examination, and patient questionnaire.

Subjects were permitted to have second eyes (fellow eyes) treated at the same time as the first eye (primary treatment). Subjects were eligible for retreatment no sooner than 3 months after surgery. Subjects were eligible for retreatment if the manifest refractive spherical equivalent was 0.5 D or greater (myopic or hyperopic), the manifest astigmatism was 0.5 D or more, the distance visual acuity was 20/30 or less, or due to any subjective complaints by the patient with treatable cause as determined by the investigator.

Effectiveness was evaluated based on improvement in uncorrected visual acuity and predictability of the manifest refraction spherical equivalent (MRSE).

Study Period, Investigational Sites and Demographic Data Hyperopia

5.2.1.1 Study Period Hyperopia

A total of 290 eyes in 151 subjects were treated between 9/24/01 and 12/11/02.

5.2.1.2 Demographics and Baseline Characteristics Hyperopia

The demographics for this study are very typical of a contemporary refractive surgery trial performed in the U.S. Gender of subjects treated was almost equally split with 51.0% (148/290) of the cases being female and 49.0% (142/290) being male. Overall, 91.4% (265/290) of eyes treated were in Caucasian subjects, 7.2% (21/290) in Hispanics, and 1.4% (4/290) were categorized as "other" races. The mean age of the patients treated was 51.6 ± 8.8 years with a range from 25 to 69.

Table 17
Demographic Characteristics
(N=290)

Category	Classification	%	n
Gender	Female	51.0	148
	Male	49.0	142
Race	Caucasian	91.4	265
	Black	0.0	0
	Asian	0.0	0
	Hispanic	7.2	21
	Other	1.4	4
	Not Reported	0.0	0
Eyes	OD	49.3	143
	OS	50.7	147
CL History	Soft	30.7	89
	RGP	3.4	10
	PMMA	0.3	1
	Glasses	65.5	190
	Unknown	0.0	0
Age (in Years)	Average	51.55	
	Standard Deviation	8.8	
	Minimum	25.0	
	Maximum	69.0	

Data Analysis and Results Hyperopia

5.2.1.3 Baseline characteristics Hyperopia

Table 18 contains a summary of the preoperative refractive errors of the entire cohort.

Table 18
Baseline Characteristics
All Eyes (n=290)

Spherical Equivalent Refraction	%	n
0.00 to 1.00 D	13.4	39
1.01 to 2.00 D	35.5	103
2.01 to 3.00 D	28.3	82
3.01 to 4.00 D	12.1	35
4.01 to 5.00 D	6.2	18
5.01 to 6.00 D	3.4	10
	1.0	3

Cylinder	%	n
0.00 D	25.5	74
0.25 D	13.4	39
0.50 D	21.7	63
0.75 D	14.5	42
1.00 D	9.3	27
1.25 D	3.8	11
1.50 D	2.1	6
1.75 D	2.1	6
2.00 D	3.1	9
2.25 D	1.4	4
2.50 D	0.7	2
2.75 D	0.0	0
3.00 D	0.3	1
3.25 D	0.3	1
3.50 D	1.0	3
3.75 D	0.0	0
4.00 D	0.3	1
4.25 D	0.0	0
4.50 D	0.3	1
4.75 D	0.0	0
>5.00 D	0.0	0

5.2.1.4 Postoperative Characteristics and Results Hyperopia

5.2.1.4.1 Patient Accountability Hyperopia

There were 290 eyes treated. Accountability for All Eyes treated was 98.3% (285/290) at 1–month, 95.2% (276/290) at 3-months, 93.9% (262/279) at 6-months, and 69.9% (100/143) at 1-year. The following cohorts were used for analysis:

- Safety-all eyes (290)
- Effectiveness-all eyes (290)
- Stability-subset of all eyes seen at any two consecutive visits, and subset of all eyes seen at 1, 3 and 6-months (279 and 249)

5.2.1.4.2 Stability of Outcome Hyperopia

In the 3-6 month window, greater than 95% of eyes experienced a change of MRSE not exceeding 1.0 D. Furthermore, the mean of the paired difference of MRSE was +0.01 D in the 3 to 6-month time period. Thus, stability was demonstrated at 6-months postoperatively.

Table 19
Refractive Stability
(Eyes with 1, 3 and 6 Month Visits (n=249)

Change in MRSE	1 and 3 Months		3 and 6 Months	
	%	n	%	n
	95% CI		95% CI	
≤1.00 D	96.0	239	98.0%	244
95% CI for %	94.8%, 97.2%		97.1%, 98.9%	
MRSE (D)				
Mean	+0.12 D		+0.01 D	
SD	0.40		0.37	
95% CI for Mean	+0.07, +0.17		-0.04, +0.05	

5.2.1.4.3 Effectiveness Outcomes Hyperopia

The analysis of effectiveness was based on the 260 eyes evaluable at the 6-month stability time point. Key efficacy outcomes over the course of the study and at the point of stability stratified by diopter of MRSE are presented in Tables 20 and 21.

Table 20
Summary of Key Efficacy Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI	1 Year % n 95% CI
Efficacy Variables	**N=232**	**N=225**	**N=212**	**N=80**
UCVA 20/20 or better*	61.6 143 58.5%, 64.8%	68.9 155 65.8%, 72.0%	67.5 143 64.2%, 70.7%	67.5 54 62.3%, 72.7%
UCVA 20/40 or better*	5.6 224 95.4%, 97.8%	96.4% 217 95.2%, 97.7%	95.3% 202 93.8%, 96.7%	98.8 79 97.5%, 100%
	N=285	**N=276**	**N=260**	**N=98**
MRSE ± 0.50 D	72.6 207 70.0%, 75.3%	71.0 196 68.3%, 73.8%	72.3 188 69.5%, 75.1%	65.3 64 60.5%, 70.1%
MRSE ± 1.00 D	5.4 269 93.0%, 95.8%	93.8 259 92.4%, 95.3%	90.4 235 88.6%, 92.2%	90.8 89 87.9%, 93.7%
MRSE ± 2.00 D	99.7 284 99.3%, 100%	99.6 275 99.3%, 100%	100 260 100%, 100%	100 98 100%, 100%

Table 21
Summary of Key Efficacy Variables at 6 Months (Stratified by Preoperative MRSE)

	0 to 1 D % n 95% CI	>1 to 2 D % n 95% CI	>2 to 3 D % n 95% CI	>3 to 4 D % n 95% CI	>4 to 5 D % n 95% CI	>5 to 6 D % n 95% CI	>6 to 7 D % n 95% CI	Total ≤7 D % n 95% CI
Efficacy Variables	**N=27**	**N=76**	**N=60**	**N=24**	**N=16**	**N=7**	**N=2**	**N=212**
UCVA 20/20 or better*	77.8 21 69.8%,85.8%	79.0 60 74.3%, 83.6%	63.3 38 57.1%, 69.6%	37.5 9 27.6%, 47.4%	50.0 8 37.5%, 62.5%	71.4 5 54.4%, 88.5%	100.0 2 100%, 100%	67.5 143 64.2%, 70.7%
UCVA 20/40 or better*	96.3 26 92.7%, 99.9%	97.4 74 95.5%, 99.2%	95.0 57 92.2%, 97.8%	91.7 22 86.0%, 97.3%	93.8 15 87.7%, 99.8%	85.7 6 72.5%, 98.9%	100.0 2 100%, 100%	95.3 202 93.8%, 96.7%
	N=37	**N=96**	**N=73**	**N=28**	**N=16**	**N=8**	**N=2**	**N=260**
MRSE ± 0.50 D	91.9 34 87.4%, 96.4%	76.0 73 71.7%, 80.4%	64.4 47 58.8%, 70.0%	71.4 20 62.9%, 80.0%	62.5 10 50.4%, 74.6%	50.0 4 32.3%, 67.7%	0.0 0 0.0%, 0.0%	72.3 188 69.5%, 75.1%
MRSE ± 1.00 D	97.3 36 94.6%, 100%	95.8 92 93.8%, 97.9%	83.6 61 79.2%, 87.9%	85.7 24 79.1%, 92.3%	100 16 100%, 100%	75.0 8 59.7%, 90.3%	0.0 0 0.0%, 0.0%	90.4 235 88.6%, 92.2%
MRSE ± 2.00 D	100 37 100%, 100%	100 96 100%, 100%	100 73 100%, 100%	100 28 100%, 100%	100 16 100%, 100%	100 8 100%, 100%	100 2 100%, 100%	100 260 100%, 100%

*For all eyes minus those intentionally treated for monovision.

Analysis of the correction of the cylindrical component of the astigmatic eyes is presented in Tables 22 and 23. The Ophthalmic Devices Panel (the Panel), at the January 14, 1997 meeting, assessed outcomes from a myopic astigmatic treatment and provided FDA with recommendations as to acceptable effectiveness rates. The mean reduction in absolute cylinder at 6-months is consistent with what the Panel considered acceptable mean reduction in absolute cylinder at the point of stability.

Table 22
Cylinder Correction Efficacy Stratified by Preoperative Cylinder

	6 Months	
Preoperative Cylinder	**Reduction of Absolute Cylinder**	
	% Reduction Mean[1]	**Ratio Mean[2]**
≤ 1.00 D	69.9%	0.63
> 1.00 to ≤ 2.00 D	75.1%	0.17
> 2.00 to ≤ 3.00 D	68.5%	0.22
> 3.00 to ≤ 4.00 D	80.7%	0.07
> 4.00 to ≤ 5.00 D	72.2%	-0.28
Total	70.9%	0.53

[1] [(Postoperative cylinder – Preoperative cylinder) / Preoperative cylinder] x 100
[2] Postoperative cylinder / Preoperative cylinder]

Looking at the intended versus achieved vector magnitude cylinder, the Intended Refractive Correction ("IRC") had a mean of –1.01 ± 0.79 D. The Surgically Induced Refractive Correction ("SIRC") had a mean of –1.09 ± 0.80 D. The vector magnitude ratio (SIRC/IRC) was 1.16 at 6-months. The Panel has found 0.82 acceptable for correction efficacy (SIRC/IRC) at stability.

Table 23
Cylinder Correction Efficacy Stratified by Preoperative Cylinder

	6 Months
Preoperative Cylinder	**Achieved vs. Intended Vector Magnitude Ratio (Achieved/Intended) Mean**
ALL	1.16
0 to 0.50 D	1.28
>0.50 to ≤ 1.00 D	1.24
>1.00 to ≤ 2.00 D	1.03
>2.00 to ≤ 3.00 D	0.98
>3.00 to ≤ 4.00 D	0.98
>4.00 to ≤ 5.00 D	0.83

5.4.1.1.1 Key Safety Results Hyperopia

The analysis of safety was based on the 260 eyes that have had the 6-month examination. The key safety results for this study are presented in Tables 24 and 25. Overall the device was deemed reasonably safe.

Table 24
Summary of Key Safety Variables Over Time

	1 Month	3 Months	6 Months	1 Year
	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI
Safety Variables	**N=285**	**N=276**	**N=260**	**N=98**
Loss of ≥ 2 lines BSCVA	3.2 9 2.1%, 4.2%	1.8 5 1.0%, 2.6%	1.5 4 0.8%, 2.3%	1.0 1 0.0%, 2.0%
BSCVA worse than 20/40	0.7 2 0.2%, 1.2%	0.4 1 0.0%, 0.7%	0.4 1 0.0%, 0.8%	0.0 0 0.0%, 0.0%
	N=92	**N=86**	**N=79**	**N=16**
Increase > 2 D Cylinder #	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=260	**N=251**	**N=241**	**N=90**
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

Table 25
Summary of Key Safety Variables at 6 Months (Stratified by Preoperative MRSE)

	0 to 1 D	>1 to 2 D	>2 to 3 D	>3 to 4 D	>4 to 5 D	>5 to 6 D	>6 to 7 D	Total ≤7 D
	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI
Safety Variables	**N=37**	**N=96**	**N=73**	**N=28**	**N=16**	**N=8**	**N=2**	**N=260**
Loss of ≥ 2 lines BSCVA	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	2.7 2 0.8%, 4.7%	0.0 0 0.0%, 0.0%	6.3 1 0.2%,12.3%	12.5 1 0.8%,24.2%	0.0 0 0.0%, 0.0%	1.5 4 0.8%, 2.3%
BSCVA worse than 20/40	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	6.3 1 0.2%,12.3%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.4 1 0.0%, 0.8%
	N=11	**N=31**	**N=29**	**N=4**	**N=3**	**N=1**	**N=0**	**N=79**
Increase >2 D cylinder#	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=36	**N=93**	**N=72**	**N=21**	**N=11**	**N=6**	**N=2**	**N=241**
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

#For eyes treated for spherical correction only.

5.4.1.1.2 Retreatment Hyperopia

A total of 16 eyes were retreated with the study laser due primarily to undercorrection. One eye was retreated for overcorrection. Table 26 contains the outcomes for retreated eyes.

Table 26
Summary of Key Safety and Efficacy Variables Over Time for Retreated Eyes

	1 Month	3 Months	6 Months	1 Year
	% n 95% CI	% n 95% CI	% n 95% CI	% n 95% CI
Efficacy Variables	**N=11**	**N=8**	**N=2**	**N=0**
UCVA 20/20 or better*	54.6 6 39.5%, 69.6%	75.0 6 59.7%, 90.3%	100 2 100%, 100%	0.0 0 0.0%, 0.0%
UCVA 20/40 or better*	100 11 100%, 100%	100 8 100%, 100%	100 2 100%, 100%	0.0 0 0.0%, 0.0%
	N=12	**N=10**	**N=3**	**N=0**
MRSE ± 0.50 D	83.3 10 72.6%, 94.1%	80.0 8 67.4%, 92.7%	66.7 2 39.5%, 93.9%	0.0 0 0.0%, 0.0%
MRSE ± 1.00 D	83.3 10 72.6%, 94.1%	90.0 9 80.5%, 99.5%	66.7 2 39.5%, 93.9%	0.0 0 0.0%, 0.0%
MRSE ± 2.00 D	91.7 11 83.7%, 99.7%	90.0 9 80.5%, 99.5%	66.7 2 39.5%, 93.9%	0.0 0 0.0%, 0.0%
Safety Variables	**N=12**	**N=10**	**N=3**	**N=0**
Loss of ≥ 2 lines BSCVA	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/40	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
	N=8	**N=7**	**N=2**	**N=0**
Increase >2 D cylinder#	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

*For all eyes minus those intentionally treated for monovision.
#For eyes treated for spherical correction only.

5.4.1.1.3 Patient Satisfaction Hyperopia

Subjects were asked to complete a patient questionnaire preoperatively and at 3-months, 6-months, and 1-year postoperatively. Responses were made by placing a mark or an "x" through the provided line. Each end of the line was marked with opposing answers such as "Never" versus "All the Time". A mark on either end of the bar represented an extreme answer (never on one end, all the time on the other end) and a mark in the middle indicated a scaled response between the extremes.

Patient reports of glare from bright lights and night driving glare improved after LASIK.

Table 27
Patient Symptoms

	Preoperative						6 Months					
	None-Mild		Moderate		Marked-Severe		None-Mild		Moderate		Marked-Severe	
	%	n	%	n	%	n	%	n	%	n	%	n
	N=287		N=287		N=287		N=260		N=260		N=260	
Glare from Bright Lights	50.9	146	27.5	79	21.6	62	65.4	170	20.8	54	13.8	36
Halos	70.4	202	15.3	44	14.3	41	71.2	185	15.0	39	13.9	36
Light Sensitivity	61.7	177	17.8	51	20.6	59	61.5	160	23.5	61	15.0	55
Visual Fluctuations	71.1	204	24.7	71	4.2	12	55.4	144	28.5	74	16.2	42
Night Driving Glare	78.0	223	10.5	30	11.5	33	83.0	216	8.5	22	8.5	22

Table 28 details changes in patient's responses to survey questions regarding symptoms. As can be seen in the table, in the majority of cases, there was no change in the patient's report of symptoms.

Table 28
Change in Patient Symptoms at 6 Months
(N=260)

	Much Worse		Somewhat Worse		No Change		Somewhat Better		Much Better	
	%	n	%	n	%	n	%	n	%	n
Glare from Bright Lights	3.0	8	8.0	21	62.9	163	19.7	51	6.4	17
Halos	6.4	17	6.8	18	68.6	178	13.6	35	4.5	12
Light Sensitivity	4.9	13	8.0	21	67.4	175	14.8	38	4.9	13
Visual Fluctuations	6.1	16	23.5	61	62.5	162	5.7	15	2.3	6
Night Driving Glare	4.2	11	11.8	31	61.2	159	12.9	34	9.9	25